TRW 1646/B EC

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: OKAMURA et al.

Application No.: 09/050,249 Conf. No. 6601

Filed: March 30, 1998

For: IFN-GAMMA PRODUCTION INDUCING PROTEIN...

Art Unit: 1646

Examiner: D. Jiang

Washington, D.C.

Atty.'s Docket: OKAMURA2B

Date: August 3, 2004

THE HONORABLE COMMISSIONER FOR PATENTS
U.S. Patent and Trademark Office
2011 South Clark Place
Customer Window, **Mail Stop: Amendment**
Crystal Plaza Two, Lobby, Room 1B03
Arlington, Virginia 22202

Sir:

Transmitted herewith is a [X] Response [ ] _____
in the above-identified application.

[ ] Small Entity Status: Applicant(s) claim small entity status. See 37 C.F.R. §1.27.

[ ] No additional fee is required.

[XX] The fee has been calculated as shown below:

	(Col. 1) CLAIMS REMAINING AFTER AMENDMENT		(Col. 2) HIGHEST NO. PREVIOUSLY PAID FOR	(Col. 3) PRESENT EXTRA EQUALS	SMALL ENTITY RATE	SMALL ENTITY ADDITIONAL FEE	OR	OTHER THAN SMALL ENTITY RATE	OTHER THAN SMALL ENTITY ADDITIONAL FEE
TOTAL	* 108	MINUS	** 108	0	x 9	$		x 18	$
INDEP.	* 4	MINUS	*** 4	0	x 43	$		x 86	$
FIRST PRESENTATION OF MULTIPLE DEP. CLAIM					+ 145	$		+ 290	$
					ADDITIONAL FEE TOTAL	$	OR	TOTAL	$

* If the entry in Col. 1 is less than the entry in Col. 2, write "0" in Col. 3.

** If the "Highest Number Previously Paid for" IN THIS SPACE is less than 20, write "20" in this space.

*** If the "Highest Number Previously Paid for" IN THIS SPACE is less than 3, write "3" in this space.

The "Highest Number Previously Paid For" (total or independent) is the highest number found from the equivalent box in Col. 1 of a prior amendment of the number of claims originally filed.

[XX] Conditional Petition for Extension of Time

If any extension of time for a response is required, applicant requests that this be considered a petition therefor.

[XX] It is hereby petitioned for an extension of time in accordance with 37 CFR 1.136(a). The appropriate fee required by 37 CFR 1.17 is calculated as shown below:

Small Entity			Other Than Small Entity		
Response Filed Within			Response Filed Within		
[ ]	First	- $ 55.00	[ ]	First	- $ 110.00
[ ]	Second	- $ 210.00	[ ]	Second	- $ 420.00
[ ]	Third	- $ 475.00	[XX]	Third	- $ 950.00
[ ]	Fourth	- $ 740.00	[ ]	Fourth	- $ 1480.00
Month After Time Period Set			Month After Time Period Set		

[ ] Less fees ($_____) already paid for ___ month(s) extension of time on _____.

[ ] Please charge my Deposit Account No. 02-4035 in the amount of $_____.

[XX] Credit Card Payment Form, PTO-2038, is attached, authorizing payment in the amount of $ 950.00.

[ ] A check in the amount of $_____ is attached (check no.).

[XX] The Commissioner is hereby authorized and requested to charge any additional fees which may be required in connection with this application or credit any overpayment to Deposit Account No. 02-4035. This authorization and request is not limited to payment of all fees associated with this communication, including any Extension of Time fee, not covered by check or specific authorization, but is also intended to include all fees for the presentation of extra claims under 37 CFR §1.16 and all patent processing fees under 37 CFR §1.17 throughout the prosecution of the case. This blanket authorization does not include patent issue fees under 37 CFR §1.18.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTY.'S DOCKET: OKAMURA=2B

In re Application of:	)	Art Unit: 1646
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OKAMURA et al.	)	Examiner: D. Jiang
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Appln. No.: 09/050,249	)	Washington, D.C.
	)	
Date Filed: March 30, 1998	)	Confirmation No. 6601
	)	
For: IFN-GAMMA PRODUCTION INDUCING PROTEIN	)	August 3, 2004

RESPONSE

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
2011 South Clark Place
Customer Window, **Mail Stop Amendment**
Crystal Plaza Two, Lobby, Room 1B03
Arlington, Virginia 22202

Sir:

This communication is responsive to the Office Action of February 11, 2004. Petition and payment for a three month extension of time are attached hereto.

The Office Action and the cited and applied reference have been carefully appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 93-96, 98-117 and 119 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention. The examiner states that newly amended claim 93 recites the limitation "a variant thereof which has the same antigenic fragment(s) as in IL-18 to be used in obtaining said monoclonal antibody" constitutes new matter because this limitation is not found in the original disclosure. This rejection is respectfully traversed.

In the Office Action of February 11, 2002, at page 3, in the last paragraph, the examiner stated:

> ... the issue is that the antibodies to the variants would undoubtedly include those which are not specific to SEQ ID NO:2 epitopes. To the extent that the claims encompass antibodies that bind to epitopes not found in the particularly disclosed sequence, there is no written description of those epitopes.

The recited limitation which the examiner considers to be new matter was introduced merely to limit the claimed antibodies to those well disclosed in the original disclosure and is not believed to add any new matter to the application. Applicants do not intend to cover antibodies which recognize some other protein having <u>different</u> antigenic fragment(s) from (i) IGIF or IL-18 as defined in claim 93.

The specification as originally filed has the following disclosures:

> ... The protein generally has a partially or totally revealed amino acid sequence, for example, the amino acid sequence containing

> the N-terminal is SEQ ID NO:3 and its homologous amino acid sequences. Variants, which have complementary amino acid sequences to the one in SEQ ID NO:3, can be obtained by replacing one or more amino acids in SEQ ID NO:3 with other amino acids without altering ("alternating" is a typographical error) the inherent biological properties of the present protein. (at page 9, third paragraph) (emphasis added). Please note that "SEQ ID NO:3" has been amended to "SEQ ID NO:2.
>
> Examples of proteins are those which have the amino acid sequence in SEQ ID NO:3 and its homologous ones. Such homologous amino acid sequences include those wherein one or more amino acids are replaced with other amino acids without substantially altering ("alternating" is a typographical error) the physicochemical properties of the present protein, as well as those which one or more amino acids are added to the N- and C-terminals in SEQ ID NO:3 (in paragraph bridging pages 15 and 16) (emphasis added).
>
> To obtain the antigenic fragments, the resultant completely- or partially-purified proteins are hydrolyzed chemically or enzymatically, or subjected to peptide synthesis using the amino acid sequence in SEQ ID NO:3. (page 16, lines 7-10) (emphasis added).

In addition to the descriptions above, applicants would like to point out the disclosure at page 20, second paragraph of the specification.

Applicants believe that these disclosures and teachings in the specification provide sufficient support for a monoclonal antibody which specifically recognizes (ii), a variant of (i), and has the same antigenic fragment(s) to be used in obtaining said monoclonal antibody.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 94, 98-117 and 119 have been rejected under 35 U.S.C. 112, second paragraph. The examiner states that the wash step is considered one of the most important steps of the hybridization, and it is the wash step that finally determines stringency. This rejection is respectfully traversed.

Applicants are of the opinion that claim 94 satisfies the requirement under 35 U.S.C. 112, second paragraph, because claim 94 is dependent from claim 93, which includes more important limitations than the wash step. Limiting the temperature of the wash step is considered by applicants too restrictive because the wash step disclosed in the specification covers a wide range of temperatures from "lower stringency" to "higher stringency".

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 93-96 and 98-118 remain rejected 35 U.S.C. 112, first paragraph. The examiner states that applicants have presented no argument towards the rejection to the broad genus of IL-18. The rejection is respectfully traversed.

Applicants would like to draw the examiner's attention to the fact that the present invention is a so-called pioneering invention, which is directed to a monoclonal antibody which

specifically recognizes a totally new substance, i.e., IL-18. The amino acid sequence and physicochemical properties of IL-18 had been first found and disclosed by applicants. Applicants therefore believes that broader protection should be given to the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 83-120 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Nakamura et al. (*Infect. Immun.* 61:64-70, 1993). The examiner indicates that Nakamura (*Infect. Immun.* 63:3966-3972, 1995) confirms that IGIF in the serum sample (75 kDa, *Infect. Immun.* 61:64-70, 1993) was proved to be the same IGIF as that found in the liver extract (19 kDa), and merely speculates that it was considered to be bound to another protein or to exist in an oligomeric form. The examiner further states that even if IGIF were bound to another protein, it would not be a limiting factor to prevent a skilled person from obtaining a monoclonal antibody to IGIF because Nakamura's factor is releatively pure, and a key step to obtaining a monoclonal antibody is to isolate a single cell line (a hybridoma) producing a monoclonal antibody to IGIF, not that the protein has to be 100% homogenous. This rejection is respectfully traversed.

Nakamura (1993) discloses nothing about a monoclonal antibody which specifically recognizes Nakamura's factor. It is

quite uncertain from the disclosure of Nakamura if a monoclonal antibody specific to Nakamura's factor can be actually obtained.

Furthermore, applicants believe that Nakamura's factor is not the same as IGIF (or IL-18) or variants thereof because Nakamura's factor reveals a molecular weight of 50-55 kDa on SDS-PAGE and 70-75 kDa using to gel filtration method, while IGIF (or IL-18) reveals 19 ± 5 kDa both on SDS-PAGE and the gel filtration method.

Even if Nakamura's factor comprises IGIF (or IL-18), the molecular weight of another protein is considered to be 56 kDa (=75 kDa -19 kDa), which is about three times the molecular weight of IGIF (or IL-18). Accordingly, if a skilled person were to try to obtain monoclonal antibodies using Nakamura's factor, the skilled person would reasonably obtain monoclonal antibodies specific to this other protein rather than a monoclonal antibody specific to IGIF (or IL-18). Furthermore, the monoclonal antibodies obtained would contain many kinds of antibodies. Therefore, it would require undue experimentation to obtain a monoclonal antibody which specifically recognizes IGIF (or IL-18) based on the disclosure in Nakamura.

It should further be noted that Nakamura never confirms the presence of IGIF having a molecular weight of 19 kDa, even if Nakamura's factor is an oligomer of IGIF. Applicants therefore believe that it would have been very difficult to obtain a

monoclonal antibody which specifically recognizes IGIF (or IL-18) based on the disclosure in Nakamura.

Although the examiner stated that the key step to obtain the monoclonal antibody is not that the protein has to be 100% homogenous. However, if the antigen used to produce antibodies includes impurities, the resultant antibodies would include many kinds of antibodies, which would undoubtedly prevent those of skill in the art from obtaining a desired monoclonal antibody without undue experimentation.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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